Micro Case 39—Vibrio Cholerae

Case

* 31 y/o man returned to the USA in late summer from a 3 wk long **trip to Bangladesh**. On the 2nd day after his return he presented with **sudden, severe, profuse, watery diarrhea**. In the ED, he passed a large **watery stool with rice water appearance**. He vomited several times and became slightly sweaty. He complained of **muscle cramps and dizziness**.
* He was on an **H2 blocker drug** for ulcer disease. Otherwise, he had always maintained good health.

**Signs and symptoms for the disease it produces.**

* sudden, severe, profuse, watery diarrhea
  + watery stool with rice water appearance
* muscle cramps and dizziness

**The source of infectious organism.**

* *Vibrio Cholerae*

**The manner of exposure, route of infection, tissues that they reside and, where appropriate, transmission to others.**

* Ingestion of contaminated water and food is the major mode of transmission
* Large bodies of fresh water contaminated by asymptomatic human carriers of V. cholerae

**The pathology and the manner by which the particular disease develops and/or is induced, including damage caused by the pathogen and damage caused by the immune system’s response to the pathogen.**

* A potent cholera toxin (CTX), an enterotoxin produced by V. cholerae, causes the severe watery diarrhea of cholera.
* A very large inoculum of organisms is required for disease, except for patients with reduced gastric acidity.
* V. cholerae lacks a genetically controlled mechanism of acid resistance; the bacteria rely on large inoculum size.
* Hypochlorhydria is a significant risk factor for cholera.
* Individuals taking antacids or other drugs that reduce gastric acidity are at risk for cholera. V. cholerae reach the small intestine in sufficient numbers and multiply and colonize the small intestine via long filamentous pili (bundles). The synthesis of pili bundles is co-regulated with the synthesis of CTX by a toxR (sensor) gene product that regulates the virulence genes. CTX is an A-B type ADP-ribosylating enterotoxin. B pentamer binds to GM1 ganglioside, a glycolipid on the surface of jejunal epithelial cells that serves as the toxin receptor and facilitates the delivery of the A subunit to its target.
* The functional A subunit activates the adenyl cyclase cascade system by irreversible transfer of an ADP-ribose subunit from NAD to membrane Gs protein, thereby raising the intracellular concentrations of cyclic AMP (cAMP) in the intestinal epithelial cells. cAMP inhibits the absorptive sodium transport system in villus cells and activates the excretory chloride transport system in crypt cells, causing
  accumulation of sodium chloride in the lumen. Watery diarrhea results from the passive movement of water into the lumen to maintain osmolality.
* Hypersecretion (fluid loss of 1 L/hr) of water and electrolytes (“rice-water diarrhea”) causes profound dehydration and associated symptoms and signs of cholera.

**Methods of identification and placement into a particular biological subset.**

* Travel History
* Fecal Exam
* Fecal cultures and gram stain
  + Comma-shaped, Gram negative rods
  + Culture on thiosulfate-citrate-bile-sucrose (TCBS) selective agar shows sucrose fermenting colonies that are yellow in appearance
* Vibrio are curved (comma-shaped), Gram negative rods.
* Highly motile, with a single flagellum
* Non-spore forming, oxidase-positive, facultative anaerobes
* The significant isolate is identifiable by biochemical tests and use of polyvalent antiseroa
* Up to 141 types of LPS-associated somatic O antigens of V. cholera are known.
* Organisms that agglutinate in 0:1 antiserum usually cause epidemics and pandemics of cholera

**Factors leading to enhanced resistance or susceptibility (e.g., recipients of vaccines, residence in geographic areas, types of work, immunodeficiency, alcoholism, age, violence/abuse, religious beliefs, etc.).**

* Individuals with achlorhydria, taking antacids or other drugs that reduce gastric acidity, are at risk of developing cholera.
* There have been 8 pandemics
  + Six out of the eight pandemics were due to the O:1 classic biotype of V. cholera.
    - The O:1 classic biotype was replaced by O:1 biotype El Tor in the seventh pandemic of cholera.
  + The eighth pandemic, due to non O:1 (O:139 Bengal)
  + Large bodies of fresh water contaminated by asymptomatic human carriers of V. cholerae are the habitats of the pathogen in the areas of the ongoing seventh pandemic (The seventh global pandemic in Asia, Africa, and Latin America)
  + Non-O:1 cholera vibrios inhabit the coastal waters of the United States (especially the Gulf coast) and cause diarrhea associated with the consumption of raw shellfish.
  + Although there have been no recent outbreaks of cholera in the United States, sporadic cases (∼5 to 10 per year) occur along the Gulf coast (mainly in Texas and Louisiana).

**Other organisms in the differential diagnosis and how to discriminate among potential causative agents.**

* Watery Diarrhea has many causes:
  + Cholera
    - Severe, acute watery diarrhea that leads to rapid dehydration is characteristic of this
    - S. Asia, Africa, and S. America are highly endemic
  + Cryptosporidiosis
  + Enterotoxic E. Coli Diarrhea (ETEC)
    - Most common cause of watery diarrhea in travelers
  + Giardiasis
  + Viral Gastroenteritis

**Prevention, treatment and vaccine design (live vs. dead).**

* Treatment
  + Fluid and electrolyte replacement
  + IV and oral rehydration
  + Antibiotic therapy is of secondary value—doxycycline is the drug of choice or a FQ (cipro)
* Prevention
  + Improved hygiene in endemic areas
  + Disease control in endemic geographic areas includes filtration and cholination of water systems and health education
* Vaccine
  + Killed cholera vaccine has limited value—partial protection for 50% of those vaccinated and protects for a short time (3-6 months)
  + No longer recommended for travelers to endemic areas